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ORIGINAL ARTICLES

Socio-demographics and clinical characteristics affecting pre-hospital delays in acute stroke patients: A 6-year registry study from a Malaysian stroke hospital

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Abstract

Background and objectives: The cumulative time spent without medical intervention in acute stroke patients may affect clinical outcomes. As the onset-to-arrival time to the hospital is crucial for effective treatment interventions, this study aimed to explore the factors associated with pre-hospital delays amongst acute stroke patients. *Methods:* We explored 932 patients data retrieved from the National Neurology Registry of Seberang Jaya Hospital between January 2013 and December 2018. Data on patient demographics and stroke manifestations were analysed using descriptive, univariate and multivariate logistic regressions. *Results:* Most patients were men (62.9%) with an average age of 62 years old. In the final multivariate regression model, pre-hospital delay was significantly lower among Chinese patients (aOR=0.6, 95% CI 0.4–0.9, p=0.016) and those using hospital ambulance (aOR=0.4, 95% CI 0.3–0.7, p<0.001), but higher among patients with lacunar infarcts (aOR=2.5, 95% CI 1.4–3.3; p<0.001). *Conclusions:* Demographic characteristic (ethnicity) and stroke manifestations, particularly stroke subtypes, and mode of transport were mainly associated with pre-hospital delays among acute stroke patients.

Keywords: acute stroke, onset-to-arrival, pre-hospital delays, patient characteristics

INTRODUCTION

Stroke remains a leading cause of disability and preventable deaths worldwide.[1] In 2005 alone, stroke accounted for 5.7 million deaths globally and this figure is projected to quadruple by 2030.[2] Efficacious time-dependent reperfusion therapies within the therapeutic window would improve clinical outcomes of patients with acute stroke.[3-6]

Early hospital arrival leads to better stroke outcomes from atherosclerosis or small-vessel occlusion by enhancing collateral blood flow or microcirculation, thus reduces disabilities of post-stroke at three months.[4,5] Early onset-to-arrival time also allows a clinician to perform comprehensive investigations in order to rule out stroke mimics and prevent misdiagnoses within the therapeutic window for acute stroke treatment.[6,7]

The ideal recommended arrival time of acute stroke patient to the hospital is three hours.[8,9] The Seberang Jaya Hospital (HSJ)'s acute stroke unit adheres to the Acute Ischemic Stroke Thrombolysis Protocol for the Ministry of Health Hospitals, in which the recommended onset-to-arrival time to the hospital should be less than 3 hours. A multitude of factors were found to significantly influence pre-hospital delays. These include severity of stroke, mode of transportation, stroke onset, lack of knowledge and socio-economic deprivation.[10-13] As the timing of hospital admission is critical to the delivery of treatment,

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with potential impacts on stroke outcomes, this study aimed to determine the factors associated with pre-hospital delays among stroke patients admitted to our centre.

METHODS

The National Neurology Registry (NNEUR) is a prospective, multicentre hospital-based registry that captures data of acute stroke patients in Malaysia (NMRR-08-1631-3189). Established in 2009, the registry is funded by the Ministry of Health Malaysia (MOH) and consists of fifteen participating stroke centres across thirteen states in Malaysia. The registry aims to capture comprehensive epidemiological surveillance data for further analytics on stroke statistics, trends, management and outcomes amongst Malaysians afflicted with stroke. The NNEUR participating stroke facilities enrolls confirmed hospitalized stroke patients within fourteen days from symptoms onset. The identification of cases is based on clinical assessment by a neurologist and radiological findings from computed tomography (CT) scans. When a patient presents with sudden onset of non-convulsive and focal neurological deficits, a CT scan of the brain is performed upon admission to the hospital to either confirm the stroke diagnosis, or to determine that the symptoms are caused by some other conditions mimicking the symptoms of stroke.[14,15]

HSJ is an acute stroke centre that provides thrombolysis therapy to patients admitted from mainland Penang.[16] The facility is the only centre from the state of Penang that participates in NNEUR. We analysed NNEUR data retrieved from this single-centre, hospital-based acute-stroke facility for the period between January 2013 and December 2018. Our main outcome measure was pre-hospital delay based on an onset-to-door time interval of 3 hours or more.[17] Onset-to-door time is the interval between symptoms onset and arrival of the patient to the emergency department (ED).[18] Patient records with unclear time of stroke onset, arrival time to the emergency department and/or whose ictus occurred during hospitalizations were excluded. Variables for analysis that were retrieved from the registry include the time taken (in hours) from the onset of stroke until the arrival to the hospital's emergency department, demographic characteristics (age, gender, ethnicity, marital status and education level), co-morbidities (diabetes, hypertension and atrial fibrillation), stroke manifestations (level of consciousness, stroke type, stroke sub-types, stroke event, previous stroke attacks and stroke severity) and mode of transport (own transport or ambulance).

Level of consciousness was measured and classified according to Glasgow Coma Scale (GCS) upon arrival with mild (13-15), moderate (9-12) and severe (3-8) scores.[19] Stroke types were classified as ischemic, transient ischemic attack (TIA) and haemorrhagic stroke. For ischemic stroke, stroke subtypes were further classified according to the Oxfordshire Community Stroke Project (OCSP) classification system that include Total Anterior Circulation Infarct (TACI), Partial Anterior Circulation Infarct (PACI), Lacunar Circulation Infarct (LACI), Posterior Circulation Infarct (PoCI) or unclassified.[20] A stroke event was categorized as first or recurrent. Stroke severity was measured using the National Institutes of Health Stroke Scale (NIHSS) and categorized as none to mild stroke (score 0-4), moderate stroke (score 5-15), moderate to severe stroke (score 16-20) and severe stroke (score 21-42).[21]

Data analysis was performed using the Statistical Package of Social Sciences (SPSS) software, version 23.0. Descriptive statistics were conducted for all variables in the study. The chi-square test was used to assess the association between pre-hospital delays (onset-to-door time interval of 3 or more hours) and categorical variables in this study. For variables with three or more categories, simple logistic regression analysis was used to obtain the odds ratio (OR). Multiple logistic regression analysis using the Backward Wald technique was performed to obtain the factors associated with pre-hospital delays among acute stroke patients. All independent variables that had significant associations with pre-hospital delays in the univariate analysis were included in the multivariate analysis. The accepted level of significance in this study was set below 0.05 ($p < 0.05$).

RESULTS

Patient characteristics

Table 1 shows demographic and clinical characteristics of acute stroke patients. Between January 2013 and December 2018, a total of 932 acute stroke patients were admitted to HSJ. Of these, 346 (37.1%) were women and 586 (62.9%) were men. The mean (±SD) age of the patients was 62 (±13) years and the majority aged above 45 years old (840, 90.1%). Most patients admitted were Malays (522, 56%) and married

(520, 84.7%). Only twelve patients (3%) were tertiary educated, while 194 (48.1%) patients of the total sample had secondary education or less. Of the three co-morbidities reported, hypertensive patients accounted for 647 (69.4%), diabetes patients accounted for 401 (43.1%) and patients who sustained atrial fibrillation accounted for 29 (3.1%) of the total sample.

The mean (±SD) duration from symptom onset to ED arrival in this study was 9 (±8.9) hours. The median (IQR) NIHSS score of the patients on admission was 4 (7). Upon arrival to the hospital, most patients had mild level of unconsciousness (736, 84.9%). The bulk of the patients sustained ischemic stroke (733, 81.8%) of lacunar type (448, 50.1%). Most cases admitted were first-ever stroke (737, 79.4%) with "none to mild severity" of illness (415, 55.4%). More patients preferred using their own transport (459, 70.2%) as compared to an ambulance (195, 29.8%) (Table 1).

Table 1: Patient characteristics (n=932)

Characteristics	n (%)
Demographics	
Gender	
Women	346 (37.1)
Men	586 (62.9)
Age group (years)	
≤45	92 (9.9)
>45	840 (90.1)
Ethnicity	
Malay	522 (56)
Chinese	285 (30.6)
Indian	125 (13.4)
Marital status, *n=614*	
Married	520 (84.7)
Single	94 (10.1)
Education level, *n=399*	
Secondary or less	192 (48.1)
Tertiary	12 (3)
Unknown	195 (48.9)
Comorbidity	
Diabetes, *n=931*	
Yes	401 (43.1)
No	530 (56.9)
Hypertension	
Yes	647 (69.4)
No	285 (30.6)
Atrial fibrillation, *n=931*	
Yes	29 (3.1)
No	902 (96.9)
Stroke manifestations	
Level of unconsciousness*, *n=867*	
Mild	736 (84.9)
Moderate	94 (10.8)
Severe	37 (4.3)
Stroke type, *n=896*	
Ischemic	733 (81.8)
Transient ischemic attack	40 (4.5)
Haemorrhagic	123 (13.7)

Characteristics	n (%)
Stroke subtypes, *n=895***	
TACI	81 (9.1)
PACI	137 (15.3)
LACI	448 (50.1)
POCI	30 (3.4)
Unclassified	33 (3.7)
Not applicable	166 (18.5)
Stroke event, *n=928*	
First	737 (79.4)
Recurrent	191 (20.6)
Previous stroke attacks	
More than 2	34 (3.6)
2 or less	898 (96.4)
Stroke severity*, *n=749***	
None to mild stroke	415 (55.4)
Moderate stroke	257 (34.3)
Moderate to severe stroke	38 (5.1)
Severe stroke	39 (5.2)
Mode of transport, *n=654*	
Own transport	459 (70.2)
Ambulance	195 (29.8)

* Level of consciousness measured by Glasgow Coma Scale, GCS 13-15 indicates mild unconsciousness, GCS 9-12 indicates moderate consciousness, GCS 3-8 indicates severe consciousness.
** Stroke subtypes were classified according to the Oxfordshire Community Stroke Project (OCSP) classification.
*** Stroke severity was measured by the National Institutes of Health Stroke Scale (NIHSS); NIHSS score was classified as 0-4 (none to mild stroke), 5-15 (moderate stroke), 16-20 (moderate to severe stroke), 21-42 (severe stroke).

Association between patient characteristics and pre-hospital delay

Table 2 exhibits the association between patient characteristics and pre-hospital delay. Pre-hospital delay was lower among the Chinese as compared to Malays (OR=0.7, 95% CI 0.5-0.9, p=0.006). Pre-hospital delay was lower among patients with moderate (OR=0.6, 95% CI 0.4-0.8, p=0.007) and severe (OR=0.4, 95% CI 0.2-0.7, p=0.002) level of unconsciousness as compared to those with a mild level of unconsciousness upon arrival to the hospital. Pre-hospital delay was lower among patients with haemorrhagic stroke as compared to those with ischemic stroke (OR=0.4, 95% CI 0.3-0.7, p<0.001). Pre-hospital delay was higher among patients with lacunar infarcts (OR=2.0, 95% 1.4-3.3, p<0.001). Pre-hospital delay was lower among patients with "moderate to severe" stroke as compared to those with "none to mild" stroke severity (OR=0.5, 95% CI 0.3-0.9, p=0.042). Pre-hospital delay was lower among patients using an ambulance as compared to those using their own transport (OR=0.4, 95% CI 0.3-0.6, p<0.001).

Factors associated with pre-hospital delays by multivariate logistic regression analyses

All statistically significant factors associated with pre-hospital delay in the univariate analyses were included in the multivariate analyses. The multivariable model retained three statistically significant factors associated with pre-hospital delay among acute stroke patients: Chinese patients (aOR=0.6, 95% CI 0.4–0.9, p=0.016), patients who sustained lacunar infarcts (aOR=2.5, 95% CI 1.4–3.3; p<0.001) and those used hospital ambulance (aOR=0.4, 95% CI 0.3–0.7, p<0.001) (Table 3).

DISCUSSION

Disparities in hospital arrival time exist between different ethnic groups.[22] This study found that pre-hospital delay was lower among the Chinese as compared to Indians or Malays. Among studies conducted in multi-ethnic countries, it was found that stroke was more prevalent among the ethnic Chinese in Singapore[23] and Malaysia.[24-26] We might conjecture that the relatively lower pre-hospital delays among the Chinese could be attributed to better stroke knowledge, concerns about

Table 2: Association between patient characteristics and pre-hospital delay

Characteristics	Arrival at hospital		OR	95% CI	p-value
	≥ 3 hours n (%)	< 3 hours n (%)			
Demographics					
Gender					
Women	231 (66.8)	115 (33.2)	1.1	0.8-1.3	0.905
Men	389 (66.4)	197 (33.6)	1		
Age group (years)					
≤45	54 (58.7)	38 (41.3)	0.7	0.4-1.1	0.094
>45	566 (67.4)	274 (32.6)	1		
Ethnicity					
Malay	363 (69.5)	159 (30.5)	1		
Chinese	171 (60)	114 (40)	0.7	0.5-0.9	0.006
Indian	86 (68.8)	39 (31.2)	0.9	0.6-1.4	0.872
Marital status					
Married	353 (67.9)	167 (32.1)	1.3	0.8-2.1	0.241
Single	58 (61.7)	36 (38.3)	1		
Education level					
Secondary or less	120 (62.5)	72 (37.5)	0.8	0.5-1.3	0.284
Tertiary	6 (50)	6 (50)	0.5	0.1-1.4	0.216
Unknown	132 (67.7)	63 (32.3)	1		
Comorbidity					
Diabetes					
Yes	277 (69.1)	124 (30.9)	1.2	0.9-1.6	0.146
No	342 (64.5)	188 (35.5)	1		
Hypertension					
Yes	425 (65.7)	222 (34.3)	0.9	0.7-1.2	0.415
No	195 (68.4)	90 (31.6)	1		
Atrial fibrillation					
Yes	18 (62.1)	11 (37.9)	0.8	0.4-1.8	0.609
No	601 (66.6)	301 (33.4)	1		
Stroke manifestations					
Level of unconsciousness					
Mild	502 (68.2)	234 (31.8)	1		
Moderate	51 (54.3)	43 (45.7)	0.6	0.4-0.8	0.007
Severe	16 (43.2)	21 (56.8)	0.4	0.2-0.7	0.002
Stroke type					
Ischemic	506 (69)	227 (31)	1		
Transient ischemic attack	26 (65)	14 (35)	0.8	0.4-1.7	0.592
Haemorrhagic	64 (52)	59 (48)	0.4	0.3-0.7	<0.001
Stroke subtype					
TACI	47 (58)	34 (42)	1.1	0.7-2	0.699
PACI	89 (65)	48 (35)	1.4	0.9-2.5	0.093
LACI	326 (72.8)	122 (27.2)	2.0	1.4-3.3	<0.001
POCI	19 (63.3)	11 (36.7)	1.4	0.6-3.3	0.422
Unclassified	22 (66.7)	11 (33.3)	1.7	0.7-5	0.236
Not applicable	92 (55.4)	74 (44.6)	1		
Stroke event					
First	483 (65.5)	254 (34.5)	0.8	0.6-1.1	0.228
Recurrent	134 (70.2)	57 (29.8)	1		
Previous stroke attacks					
More than 2	24 (70.6)	10 (29.4)	1.2	0.6-2.6	0.609
2 or less	596 (66.4)	302 (33.6)	1		

Characteristics	Arrival at hospital		OR	95% CI	p-value
	≥ 3 hours n (%)	< 3 hours n (%)			
Stroke severity					
None to mild stroke	296 (71.3)	119 (28.7)	1		
Moderate stroke	167 (65)	90 (35)	0.8	0.6-1.1	0.085
Moderate to severe stroke	21 (55.3)	17 (44.7)	0.5	0.3-0.9	0.042
Severe stroke	24 (61.5)	15 (38.5)	0.6	0.3-1.3	0.203
Mode of transport					
Own transport	195 (42.5)	264 (57.5)	1		
Ambulance	45 (23.1)	150 (76.9)	0.4	0.3-0.6	<0.001

symptoms and health seeking-behaviours, and that ethnic groups with higher risks of being afflicted with stroke would arrive early to the hospital.[22]

In contrast, other demographic characteristics such as age, gender, education level and marital status were not significantly associated with pre-hospital delays. These findings were consistent with previous studies from Japan[27], Taiwan[28] and the USA[29,30], but contrary to studies from China[30], Italy[31] and India.[32] It should be noted that demographic variables are often influenced and confounded by geographic and socio-economic variations across different populations worldwide, causing probable associations with pre-hospital delays among stroke patients to vary across countries and settings. In this study, we found that co-morbidities among stroke patients suffering from diabetes, hypertension and/or atrial fibrillation were not significantly associated with pre-hospital delays. These findings were in accordance with results from a previous study.[33] This may be due to patient's inability to identify stroke signs and symptoms with pre-existing diseases. A study from India showed that patients with a history of atrial fibrillation have better awareness of stroke symptoms, thus arrive early to the hospital.[34]

Altered consciousness level was found to be associated with pre-hospital delays among acute stroke patients.[35,36] In this study, we found that pre-hospital delays were lower among patients with moderate and severe levels of consciousness as compared to those with a mild level of consciousness. Similar findings were found in previous studies.[11,37,38] Such findings are anticipated when caregivers, relatives, colleagues or bystanders observe stroke afflicted patients losing consciousness and call emergency medical services (EMS) quickly for rapid transportation to the hospital.[38]

Additionally, we found that patients with haemorrhagic stroke were more likely to arrive

Table 3: Factors associated with pre-hospital delays (Backward Wald)

Characteristics	B	SE	Wald	Exp (B)	95% CI	p-value
Ethnicity						
Malay	Ref	Ref	Ref	Ref	Ref	Ref
Chinese	0.4	0.2	5.8	0.6	0.4-0.9	0.016
Indian	0.1	0.2	0.1	0.9	0.6-1.5	0.783
Stroke subtype						
TACI	-0.1	0.3	0.1	1.1	0.6-2	0.745
PACI	-0.5	0.3	3.4	1.7	0.9-3.3	0.064
LACI	-0.9	0.2	12.9	2.5	1.4-3.3	<0.001
POCI	-0.4	0.5	0.6	1.4	0.6-3.3	0.439
Unclassified	-0.5	0.5	0.9	1.7	0.6-5	0.350
Not applicable	Ref	Ref	Ref	Ref	Ref	Ref
Mode of transport						
Own transport	Ref	Ref	Ref	Ref	Ref	Ref
Ambulance	-0.9	0.2	11.5	0.4	0.3-0.7	<0.001

* Variables entered: All significant variables in univariate analysis.

** Exp(B) gives the adjusted Odds Ratio (aOR)

early to the hospital as compared to patients with ischemic stroke. Such association may be attributed to the severity of stroke type as haemorrhagic stroke patients experience more rapid and severe clinical manifestations, such as enlarged pupils, distress, acute onset of headache, lower level of consciousness, seizures, and eye gaze disorder.[39] Although this finding was statistically significant at the univariate level, it was eliminated in the multivariable model. A bulk of previous studies found similar trends.[30,32,40-43]

In this study, we found that patients with lacunar infarct (LACI) were more likely to arrive late to the hospital and this association was statistically significant. Similar consistency was observed in a previous study.[37] Such findings could be attributed to the fact that LACI is a non-large stroke, as defined in the OCSP classification, and has fewer salient features as compared to other larger infarcts.[44] In addition, about 10% of patients with such stroke sub-types present silent clinical features, hence patients and the people around them are often completely unaware that the patient is suffering from a stroke.[45,46]

In addition, previous studies from Japan and Korea found that patients with moderate to severe stroke (based on NIHSS score of 16-20) were more likely to arrive early to the hospital.[27,28] Our study found similar results. It could be postulated that altered levels of consciousness and stroke severity, both of which exhibits the hallmark of stroke symptomatology could be the fundamental reason to arrive early to hospital. Lastly, our study also found that stroke patients who used an ambulance were less likely to arrive late to the hospital. This finding was consistent with previous studies.[10-13,28,47-49]

In conclusion, ethnicity, stroke subtypes and mode of transportation were the three most important significant factors associated with pre-hospital delays among stroke patients in our cohort. The main strength of this study was its large, six-year sample cohort from the official hospital-based stroke registry that was set up to collect information on patient visits to the hospital for acute stroke management. We hope that these findings will be used to improve public awareness on stroke symptoms and the importance to seek immediate medical help, as soon as possible, using EMS ambulance services.

This study had several limitations. First, it was a single-centre hospital-based study that focused mainly on urban patients; the situation for acute stroke incidence in rural and remote areas was not addressed, hence extrapolation of study findings was not possible. Patients who did not seek treatment or received treatment elsewhere (for example in a private setting) were not captured in the registry and patients who died before arriving to the hospital were not included. The onset-to-arrival time may have been overestimated in certain patients, especially those with wake-up stroke. Future studies are recommended to execute a more representative, multi-centre analysis to overcome these unanswered questions for generalizable results.

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DISCLOSURE

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